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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/053,535	01/15/2002	Augustine M. Choi	13681-003002	7091

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EXAMINER
CHOI, FRANK I

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 07/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/053,535	CHOI ET AL.	
	Examiner	Art Unit	
	Frank I Choi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3,5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 42-69 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of rats having the disease states and/or conditions specifically treated and treatment specifically related to the mechanisms by which the active components effect said treatment of said disease state and/or condition which are set forth in the examples in pages 16-34 of the Specification, does not reasonably provide enablement for treatment of any and all patients, including humans, oxidative stress in general, the list of conditions or disease states set forth in Claims 42-52,57,58,60-69, or inflammation in general, including inflammation of the kidneys, brain, heart, liver, spleen, skin and lungs or secondary to sepsis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims

The claimed invention does not appear to be currently recognized as a treatment for the various conditions and disease states in humans. Further, the working examples are limited to rats and the effects are observed either in lungs or on single cells, i.e. muscle cells or macrophages. It is asserted that the methods will treat a wide range of conditions and/or disease states; however, the disclosure does not appear to indicate what exactly is being treated, i.e., symptoms, underlying mechanisms, underlying disease, secondary problems associated with

underlying disease, etc. Further, the conditions and disease states listed are in many cases not a single specific disease but represent a broad catagory of a number of disease having different etiologies, symptoms and/or treatments. Also, it appears that the active compounds are inhaled, however, other than the lungs there does not appear to be set forth in the disclosure how the compounds, in therapeutically effective amounts, reach the intended site be it kidneys, brain, heart, liver, spleen, skin, or systemically in general.

Finally, it is well-known that carbon monoxide is a deadly poison and that oxygen can cause pulmonary toxicity (Cecil Textbook of Medicine (2000), Vol. 1, pgs. 425-427). Concentrations of carbon dioxide, including concentrations falling with the claimed ranges are known to seriously impair oxygen hemoglobin binding capacity (The New Encyclopaedia Britannica (1994), Vol. 26 pg. 756). As such, the therapeutic window, if any, is extremely narrow. For instance, it has been suggested that excessive generation of carbon monoxide participates in the pathogenesis of Alzheimer's (Schipper et al., Abstract). Also, it is noted that the concentration of the gaseous components are claimed, however, concentration does not appear to adequately indicate how much of the gas is being administered and/or the effective amount of gas necessary to effect treatment. Clearly, flow rate and duration of administration effect the amount of gas administered and, consequently, the therapeutic and/or toxic effect on the patient. However, the disclosure, other than as specifically set forth in the examples, does not appear to indicate the flow rate and duration of administration or level of gas present in patient necessary to effect treatment relative to treatment of the claimed diseases and conditions (See The Merck Index, pg. 655, Asthma, O_2 Therapy). Examiner notes that current medications used in the treatment of the various disease states and/or conditions are not known to possess

treatment efficacy for any and all symptoms, and in a number of conditions and/or disease states, treatment is limited to alleviating symptoms or slowing the progression of the disease without treating the disease itself (Cecil Textbook of Medicine (2000), Vol. 1, pgs. 273-279, 357-372, 387-419, 425-427,436-448, 466-475, 507-512, 1060-1074; Cecil Textbook of Medicine (2000), Vol. 2, pgs. 1492-1499, 2042-2047, 2079-2081). As late as 1999, in a paper published by two of the inventors, the paper indicated that it may not be possible to prove that endogenous CO mediates the protective effects of HO-1 in vivo and there was only a possibility that inhalation of CO would be useful in other inflammatory disease states and that further experimentation was necessary. (Otterbein et al. (1999), pg. L693). See also Grau et al. (1992), pg. 423 (indicating that there is a great difference humans and rodents and that acute exposure to carbon monoxide increased tumor cell survival); Siow et al. (1999), pg. 388 (indicating that the effects of carbon monoxide on vascular smooth muscle relaxation are blood vessel and species specific, with findings differing from one study to another); Ringel et al. (1972), Abstract (indicating that exposure to carbon monoxide can cause parkinsonism); Schipper et al. (1995), Abstract (indicating that carbon monoxide may participate in the pathogenesis of Alzheimer's); and Stephens (1933), Abstract (indicating that exposure to carbon monoxide increased risk of occupational cancers). In light of the above, it is highly unlikely that administration of carbon monoxide would be effective for the treatment of all the disease states or conditions set forth in the claims. As such, it appears that a skilled artisan would be required to do undue experimentation in order to make and/or use the invention commensurate in scope with the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 42-69 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The concentration of the components making up the gas does not adequately indicate how much of the therapeutic gas is being administered. In light of the toxic nature of the gases being introduced the claims should indicate rate and duration of administration and/or standardized measurement of the amount of gas administered in vivo.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 69 is rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Abidin et al. (Abstract).

Abidin et al. expressly disclose a method of treating hyperoxia with carbon monoxide falling within the scope of applicant's claims (Abstract).

Alternatively, at the very least the claimed invention is rendered obvious within the meaning of 35 USC 103, because the prior art discloses products and uses that contain the same exact ingredients/components as that of the claimed invention. See In re May, 197 USPQ 601, 607 (CCPA 1978). See also Ex parte Novitski, 26 USPQ2d 1389, 1390-91 (Bd Pat. App. & Inter. 1993).

Claims 42-47, 50-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/08523 in view of Choi et al. (1996), Lefer et al. (1993) and Vassalli et al. (1998) ~~and Abidin et al.~~

WO 98/08523 teaches methods of treating inflammatory processes in humans and animals with mixtures of gases, including carbon monoxide, nitric oxide and nitrous oxide, which is effective in treating cancer, pneumonia, asthma, acute respiratory distress syndrome, pulmonary hypertension, bronchitis and sepsis (See entire document).

Choi et al. (1996) teaches that oxidative stress plays a central role in the pathogenesis of many pulmonary diseases including adult respiratory distress syndrome, emphysema, asthma, bronchopulmonary displasia and interstitial pulmonary fibrosis (Abstract).

Lefer et al. (1993) teach that carbon monoxide has cytoprotective effective in low concentrations in inflammatory states (Abstract).

Vassalli et al. (1998) teaches that carbon monoxide inhibits acute pulmonary vasoconstriction and would be effective in the treatment of acute pulmonary hypertension (Abstract).

The difference between the prior art and the claimed invention is that the prior art does not expressly disclose a method of treating the claimed disorders which are secondary or resulting from oxidative stress, a method of treating asthma, a method of treating cancer, a method of treating inflammation in at least one organ, a method of treating inflammation secondary to sepsis or sepsis or a method of promoting wound healing, with carbon monoxide. However, the prior art amply suggests the same as it is known that oxidative stress plays a central role in pulmonary disorders and that carbon dioxide is effective in treating various

conditions, including inflammation, hypertension and vasoconstriction and sepsis. As such, it would have been well within the skill of and one of ordinary skill in the art would have expected that administration of carbon dioxide would be effective in treating the above conditions.

Conclusion

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machines are (703) 308-4556 or (703) 305-3592.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (703) 308-0067. Examiner maintains a flexible schedule. However, Examiner may generally be reached Monday-Friday, 8:00 am – 5:30 pm (EST), except the first Friday of the each biweek which is Examiner's normally scheduled day off.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Mr. José Dees, can be reached on (703) 308-4628. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (703) 308-1235 and (703) 308-0198, respectively.

FIC
July 27, 2002

JOHN PAK
PRIMARY EXAMINER
GROUP 1600